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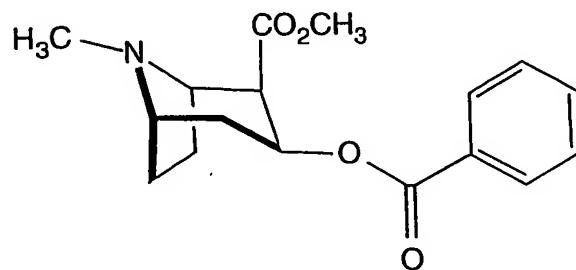
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(-)-COCAINE

FIG. 1A

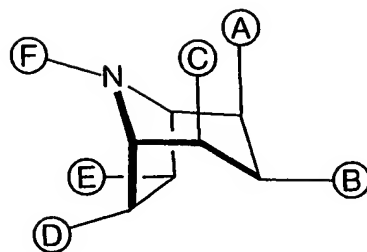


FIG. 1B

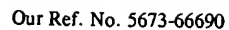
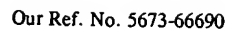
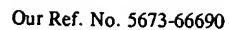
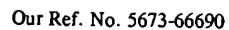
CJ#

Branch

CJ 0	Q	Q = H, OH, CH <sub>2</sub> , HALOGEN, COOH, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 1	(CH <sub>2</sub> ) <sub>n</sub> Q	Q = H, COOH, HALOGEN, 2-NITRO-4-SULFOPHENYL ESTER, N-OXYSUCCINIMIDYL ESTER, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN, CJ 1.2
CJ 1.1	CO <sub>2</sub> Q	Q = H, CH <sub>3</sub>
CJ 1.2	COQ	Q = H, HALOGEN, 1-OXY-2-NITRO-4-SULFOPHENYL, N-OXYSUCCINIMIDYL, N-MALEIMIDYL, CARRIER PROTEIN, CJ 10
CJ 2	OCO(CH <sub>2</sub> ) <sub>n</sub> Q	Q = COOH, HALOGEN, 2-NITRO-4-SULFOPHENYL ESTER, N-OXYSUCCINIMIDYL ESTER, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 2.1	OCOCH=Q	Q = H
CJ 2.2	OCOCH(O)CH <sub>2</sub>	
CJ 2.3	OCO(CH <sub>2</sub> ) <sub>n</sub> CH(O)CH <sub>2</sub>	
CJ 3	CO(CH <sub>2</sub> ) <sub>n</sub> COQ	Q = H, OH, HALOGEN, 1-OXY-2-NITRO-4-SULFOPHENYL, N-OXYSUCCINIMIDYL, N-MALEIMIDYL, CARRIER PROTEIN, CJ 10
CJ 3.1	CO(CH <sub>2</sub> ) <sub>n</sub> CNQ	Q = OCH <sub>3</sub> or CARRIER PROTEIN
CJ 4	OCO(CH <sub>2</sub> ) <sub>n</sub> COQ	Q = H, OH, HALOGEN, 1-OXY-2-NITRO-4-SULFOPHENYL, N-OXYSUCCINIMIDYL, N-MALEIMIDYL, CARRIER PROTEIN, CJ 10
CJ 4.1	CO(CH <sub>2</sub> ) <sub>n</sub> CNQ	Q = OCH <sub>3</sub> or CARRIER PROTEIN
CJ 5	CH <sub>2</sub> OCO(CH <sub>2</sub> ) <sub>n</sub> COQ	Q = H, OH, HALOGEN, 1-OXY-2-NITRO-4-SULFOPHENYL, N-OXYSUCCINIMIDYL, N-MALEIMIDYL, CARRIER PROTEIN, CJ 10
CJ 5.1	CO(CH <sub>2</sub> ) <sub>n</sub> CNQ	Q = OCH <sub>3</sub> or CARRIER PROTEIN
CJ 6	CONH(CH <sub>2</sub> ) <sub>n</sub> Q	Q = H, COOH, HALOGEN, 2-NITRO-4-SULFOPHENYL ESTER, N-OXYSUCCINIMIDYL ESTER, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 7	Y(CH <sub>2</sub> ) <sub>n</sub> Q	Y = S, O, NH; Q = HALOGEN, COOH, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 7.1	CH <sub>2</sub> Y(CH <sub>2</sub> ) <sub>n</sub> Q	Y = S, O, NH; Q = HALOGEN, COOH, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 8	OCOCH(OH)CH <sub>2</sub> Q	Q = CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 8.1	OCO(CH <sub>2</sub> ) <sub>n</sub> CH(OH)CH <sub>2</sub> Q	Q = CARRIER PROTEIN, MODIFIED CARRIER PROTEIN
CJ 9	OCOC <sub>6</sub> H <sub>5</sub>	
CJ 11	YCO(CH <sub>2</sub> ) <sub>n</sub> COQ	Y = S, O, NH; Q = OH, CARRIER PROTEIN, MODIFIED CARRIER PROTEIN or HALOGEN

FIG. 2A

Our Ref. No. 5673-66690



Our Ref. No. 5673-66690

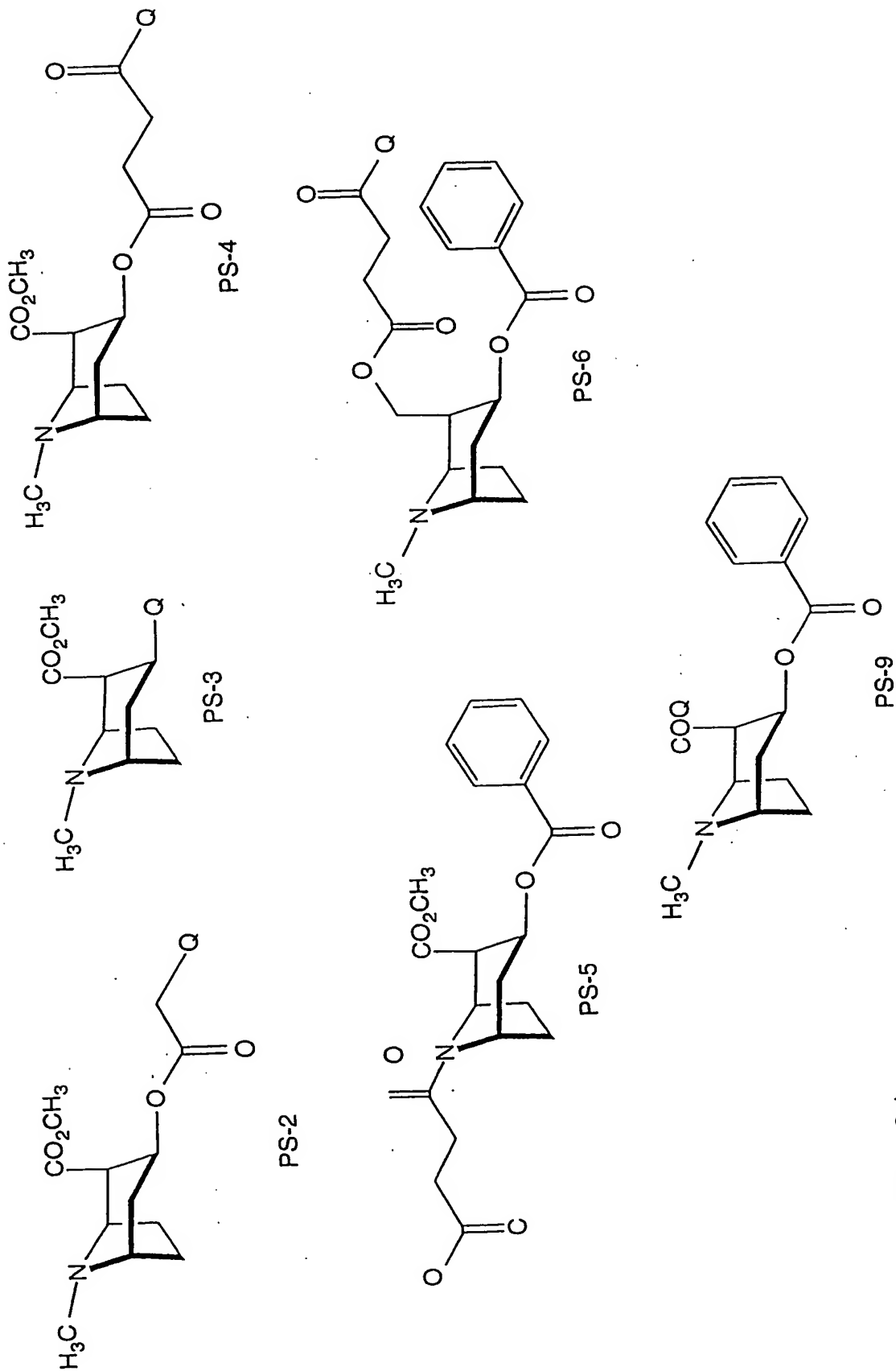


FIG. 3A

BRANCHES					
	A	B	C	D	E
					F
PS-2	CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2 WHERE Q= HALOGEN OR MODIFIED T CELL EPIOTOPE CONTAINING CARRIER AND n=1	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-3	CJ1.1 WHERE Q=CH <sub>3</sub>	CJ0 WHERE Q= MODIFIED T CELL EPIOTOPE CONTAINING CARRIER	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-4	CJ1.1 WHERE Q=CH <sub>3</sub>	CJ4 WHERE Q= MODIFIED T CELL EPIOTOPE CONTAINING CARRIER AND n=1	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-5	CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-6	CJ5 WHERE Q=CARRIER PROTEIN AND n=2	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-9	CJ1.2 WHERE Q=CARRIER PROTEIN	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-10	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2 WHERE Q=HALOGEN	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-11	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2 WHERE Q = MODIFIED T CELL EPIOTOPE CONTAINING CARRIER	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
PS-12	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2.1	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H

FIG. 3B(1)

PRECUSORS/CONJUGATES

BRANCHES					
PS-13	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2 Q=CARRIER PROTEIN OR MODIFIED T CELL EPIOTOPE CONTAINING CARRIER AND n=2	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-14	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2.2	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-15	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ8	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-16	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ2.3	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-17	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ8.1	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-18	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ4	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-19	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CL 1 WHERE Q=COOH, HALOGEN, 2-NITRO-4- SULFOPHENYL ESTER, N- OXYSUCCINIMIDYL ESTER, CARRIER PROTEIN OR MODIFIED CARRIER	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-20	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ7	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-21	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ3

FIG. 3B(2)

PRECUSORS/CONJUGATES

BRANCHES						
PS-22	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=CJ1.2
PS-23	CJ5	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H
PS-24	CJ7.1	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H
PS-25	CJ7	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H
PS-26	CJ1.2	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H
PS-27	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ2	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-28	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CL1 WHERE Q=COOH, HALOGEN 2-NITRO-4-SULFOPHENYL ESTER, N-OXY-SUCCINIMIDYL ESTER, CARRIER PROTEIN, MODIFIED T CELL EPITOPE CONTAINING CARRIER, CJ1.2	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-29	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ2.2	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-30	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ8	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-31	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ2.3	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1

FIG. 3B(3)

PRECURSORS/CONJUGATES

BRANCHES						
PS-32	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ8.1	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-33	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ4	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-34	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ5	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-35	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ2	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-36	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CL1 WHERE Q= COOH, HALOGEN 2-NITRO-4- SULFOPHENYL ESTER, N-OXY- ESTER, CARRIER SUCCINIMIDYL PROTEIN, MODI- FIED T CELL EP- ITOPE CONTAIN- ING CARRIER, CJ1.2	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-37	CJ6 WHERE Q=H OR CL1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ2.2	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-38	CJ6 WHERE Q=H OR CL1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ8	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-39	CJ6 WHERE Q=H OR CL1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ2.3	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1

FIG. 3B(4)

PRECURSORS/CONJUGATES

BRANCHES						
PS-40	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ8.1	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-41	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ4	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-42	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ5	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-43	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ2	CJ1 WHERE Q=H, n=1
PS-44	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CL1 WHERE Q=COOH, HALOGEN 2-NITRO-4-SULFOPHENYL ESTER, N-OXY-SUCCINIMIDYL ESTER, CARRIER PROTEIN, MODIFIED T CELL EP-ITOPE CONTAINING CARRIER, CJ1.2	CJ1 WHERE Q=H, n=1

↑  
PRECUSORS/CONJUGATES

FIG. 3B(5)

BRANCHES					
PS-45	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-46	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-47	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-48	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-49	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
PS-50	CJ6 WHERE Q=H OR CJ1.1 WHERE Q=CH <sub>3</sub>	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
↑ PRECUSORS/CONJUGATES					

FIG. 3B(6)

	A	B	C	D	E	F
COCAINE	CJ1.1 WHERE Q=CH3	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
ECOGONINE METHYL ESTER	CJ1.1 WHERE Q=CH3	CJ10 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1
NORCOCAINE	CJ1.1 WHERE Q=CH3	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H
BENZOYL ECOGONINE	CJ0 WHERE Q=COOH	CJ9	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ0 WHERE Q=H	CJ1 WHERE Q=H, n=1

FIG. 4

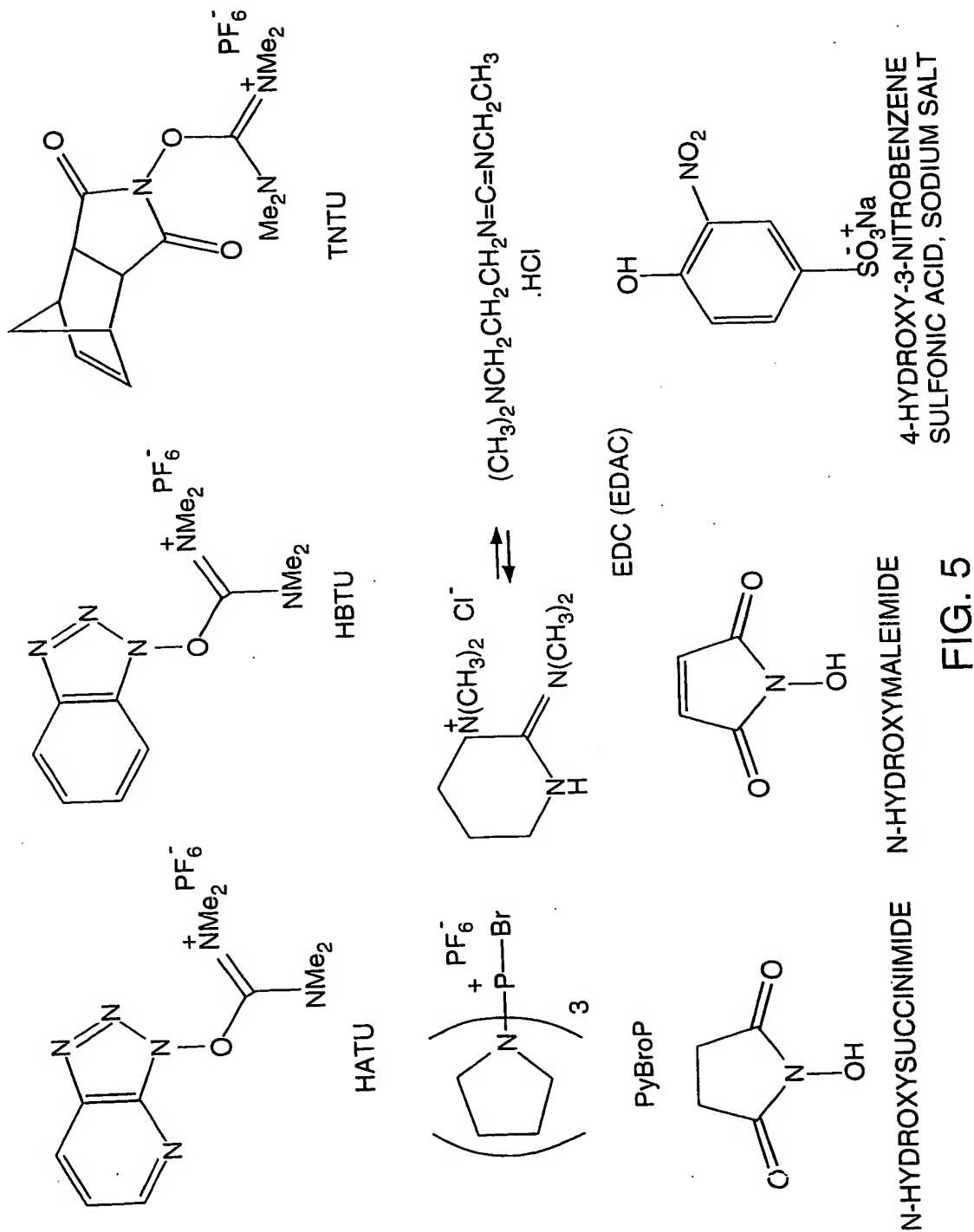
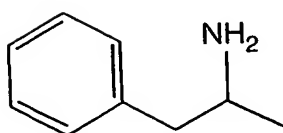
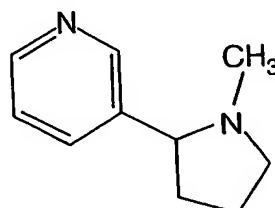


FIG. 5

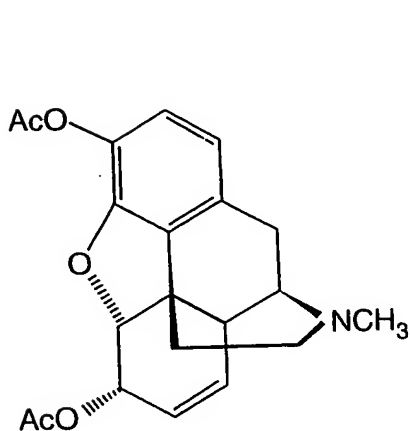
## OTHER COMMONLY ABUSED DRUGS



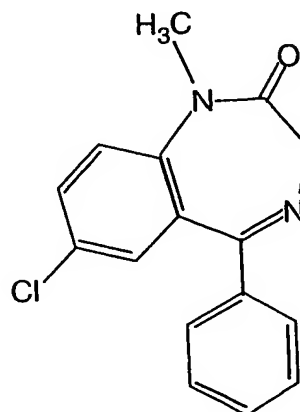
AMPHETAMINE



NICOTINE



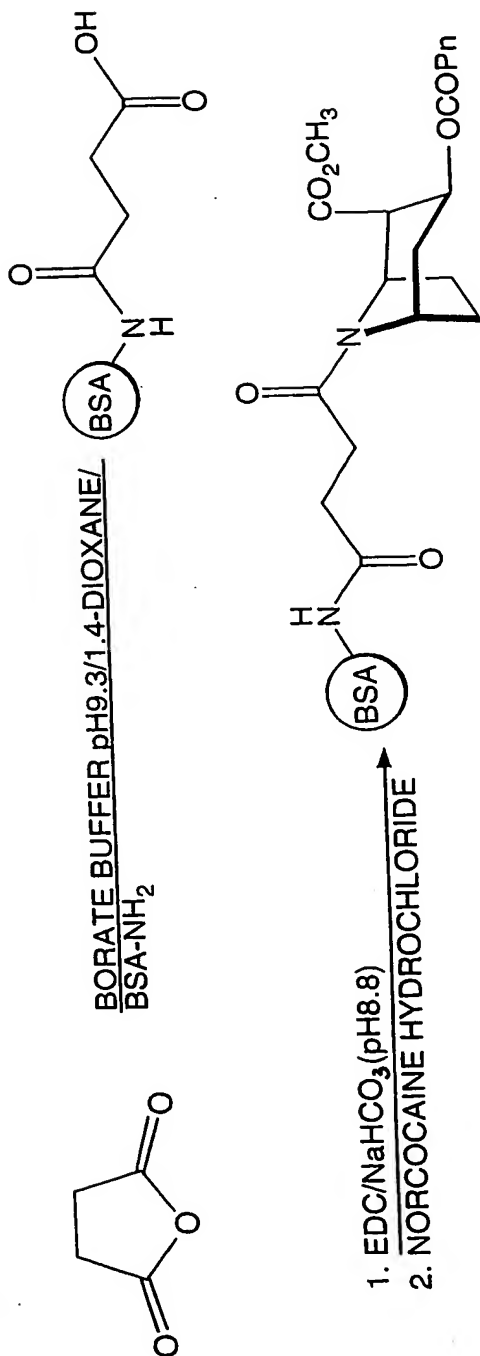
HEROIN



DIAZEPAM

FIG. 6

## METHOD A



## METHOD B

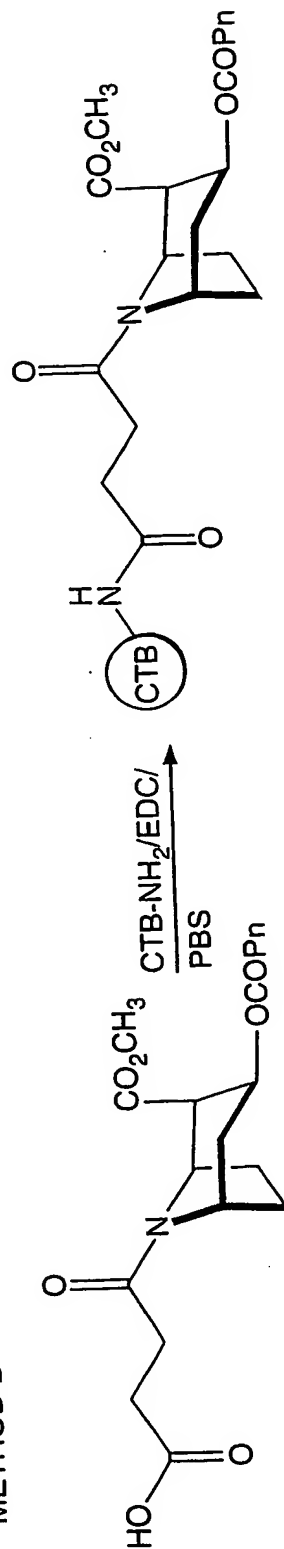


FIG. 7

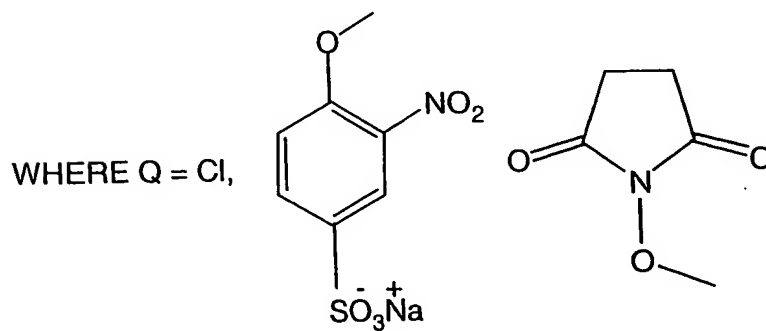
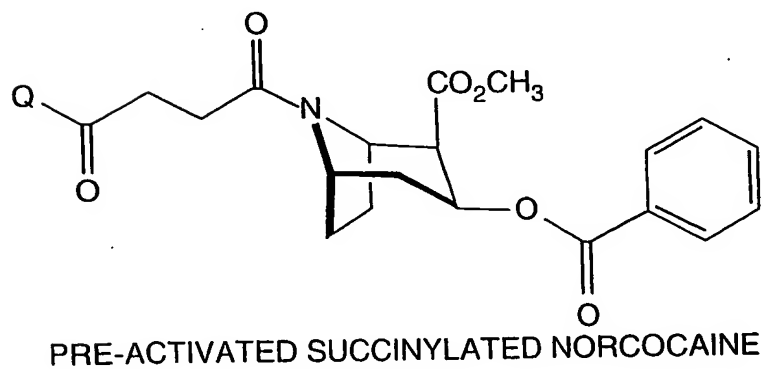
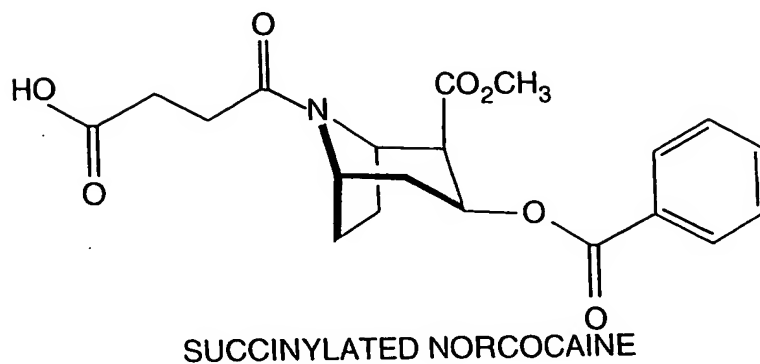


FIG. 8

FIG. 9A

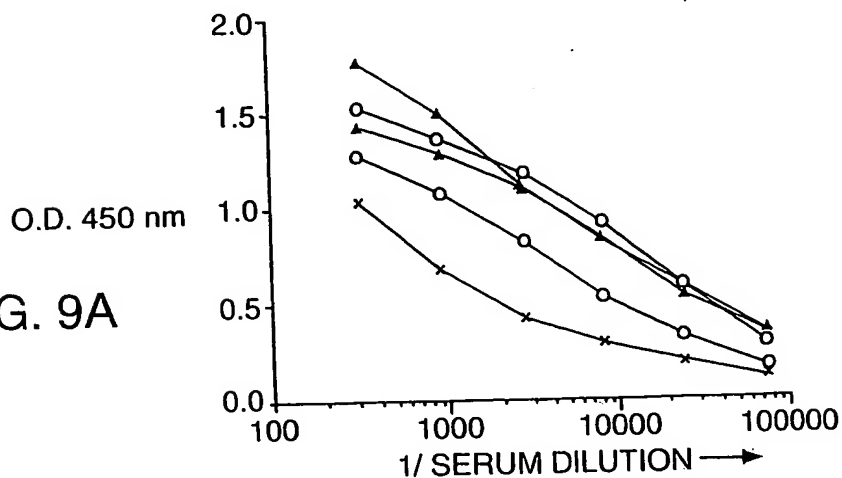


FIG. 9B

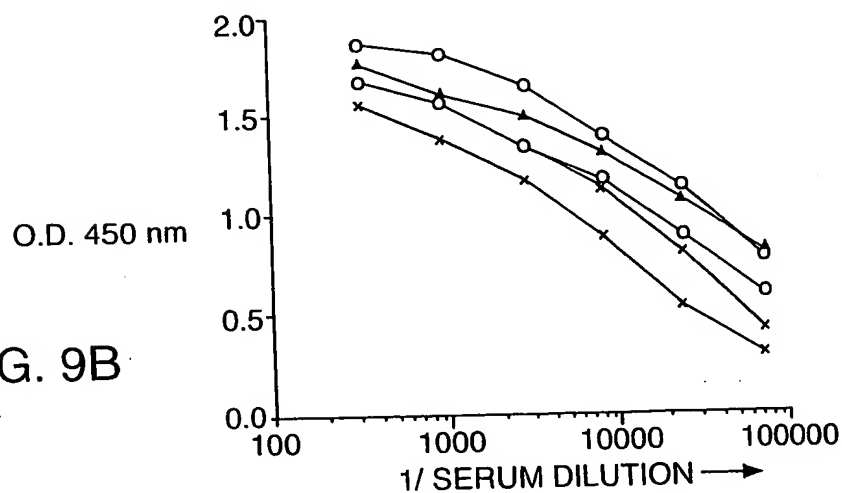
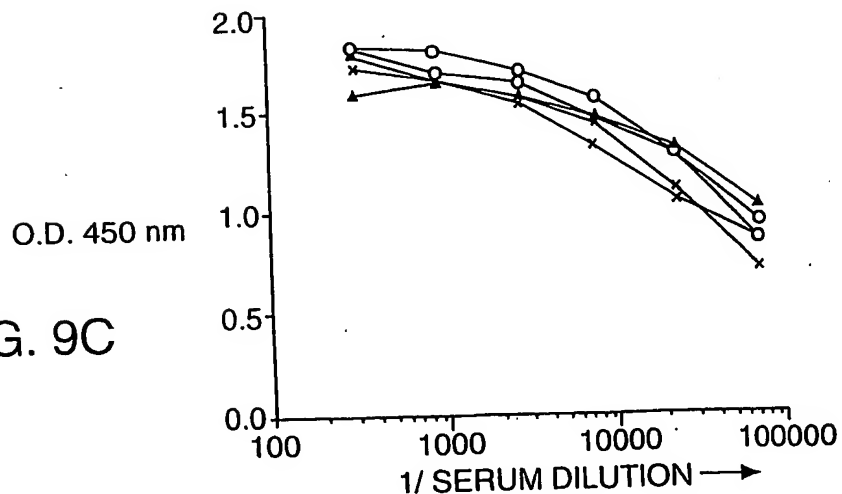


FIG. 9C



Klarquist Sparkman, LLP

For: HAPTEN-CARRIER CONJUGATES FOR USE IN DRUG-ABUSE THERAPY  
AND METHODS FOR PREPARATION OF SAME

121 SW Salmon Street, Suite 1600

Portland, Oregon 97204

Telephone: 503/226-7391

Express Mail Label EV339203081, mailed: August 22, 2003

Sheet 17 of 37

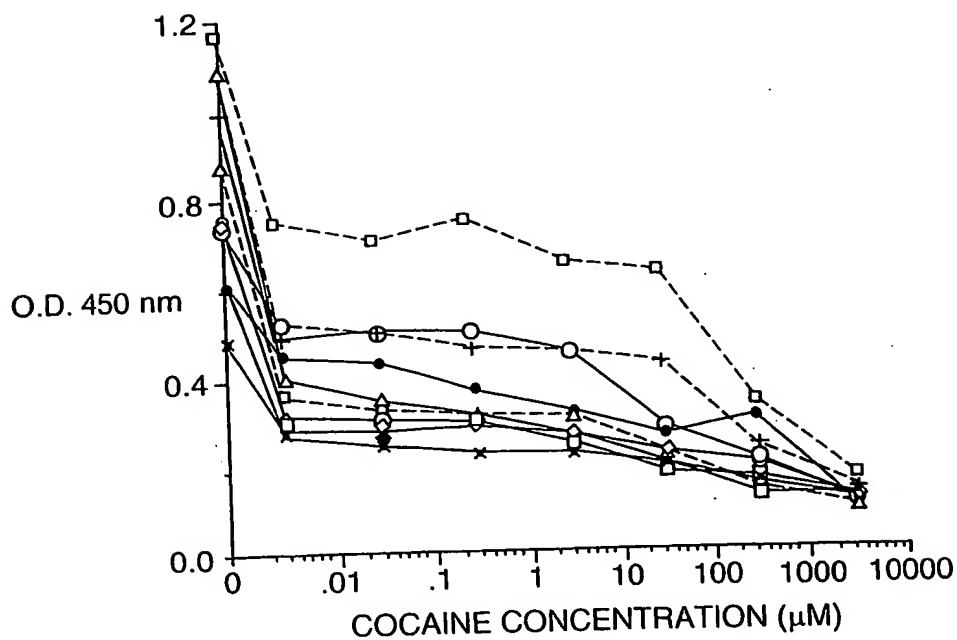


FIG. 10A

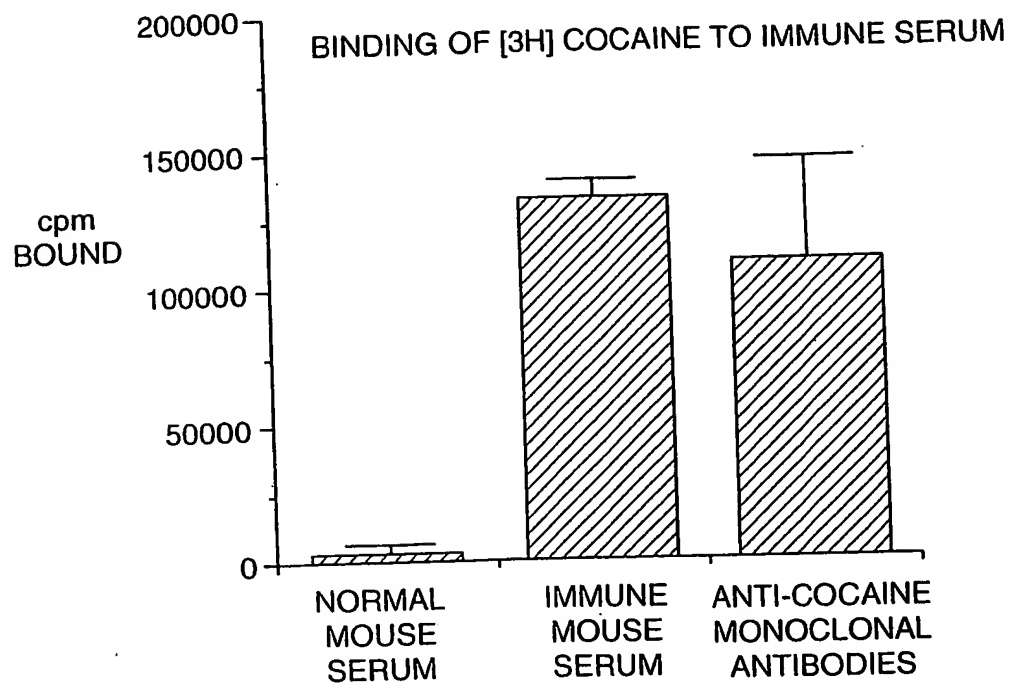


FIG. 10B

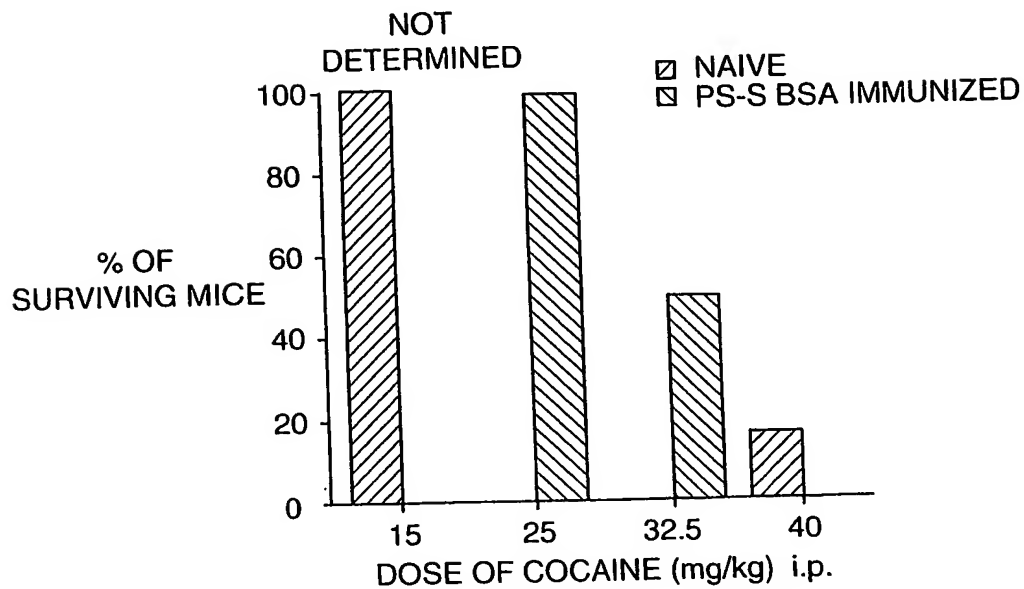


FIG. 11A

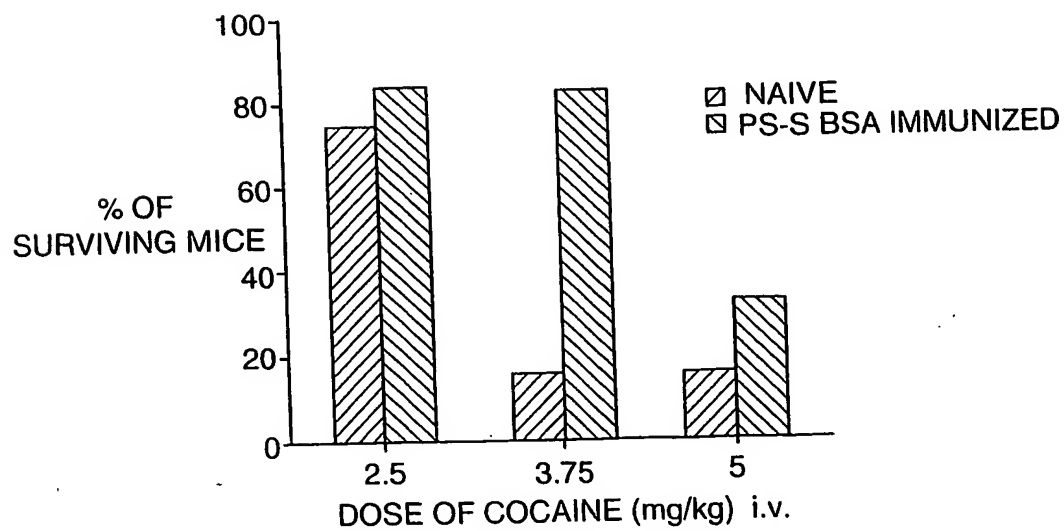
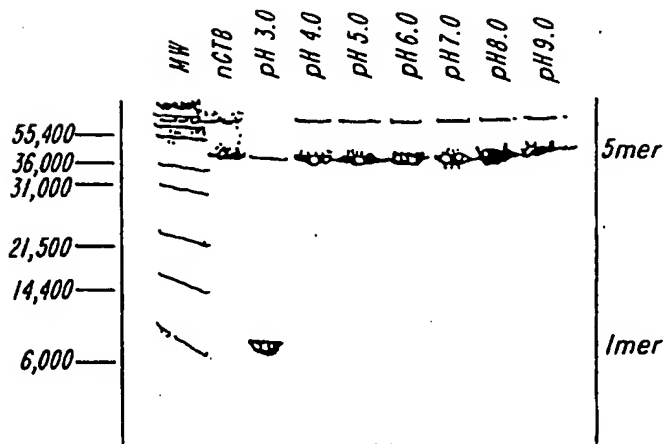
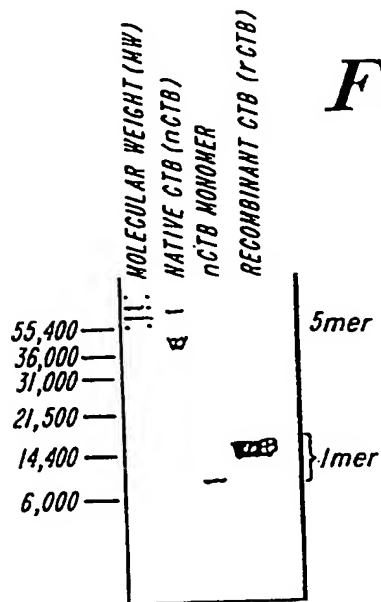
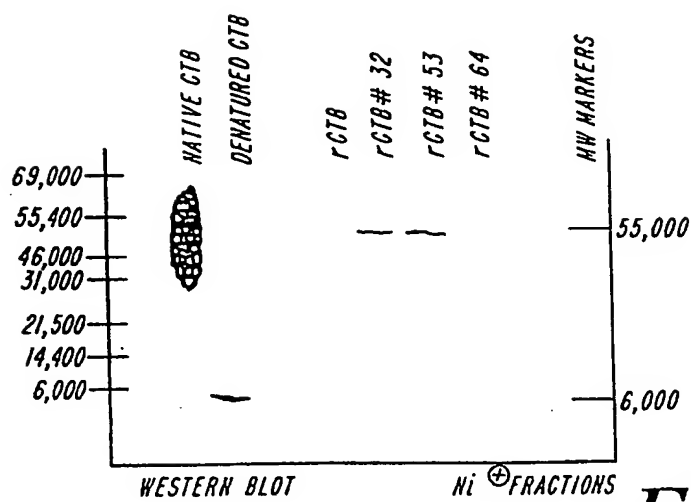
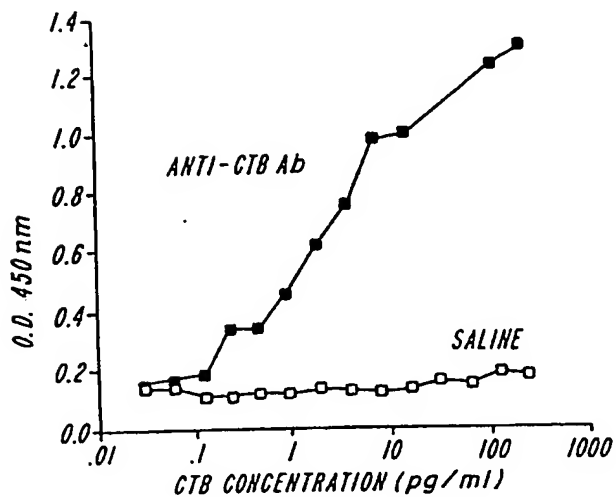


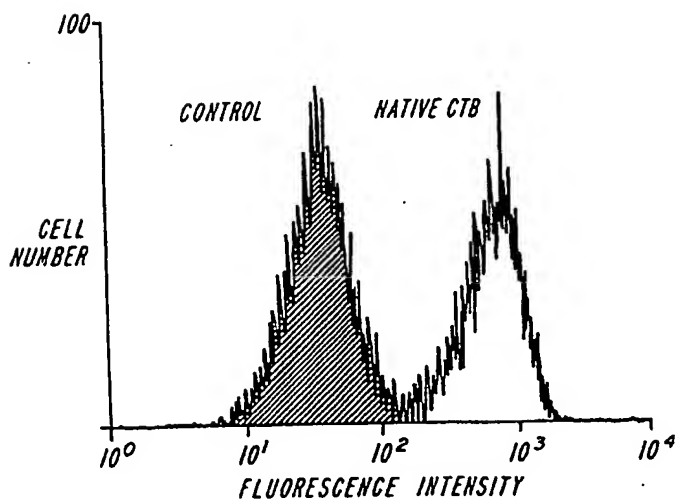
FIG. 11B

**FIG. 12B**

**FIG. 12C**



**FIG. 13A**



**FIG. 13B**

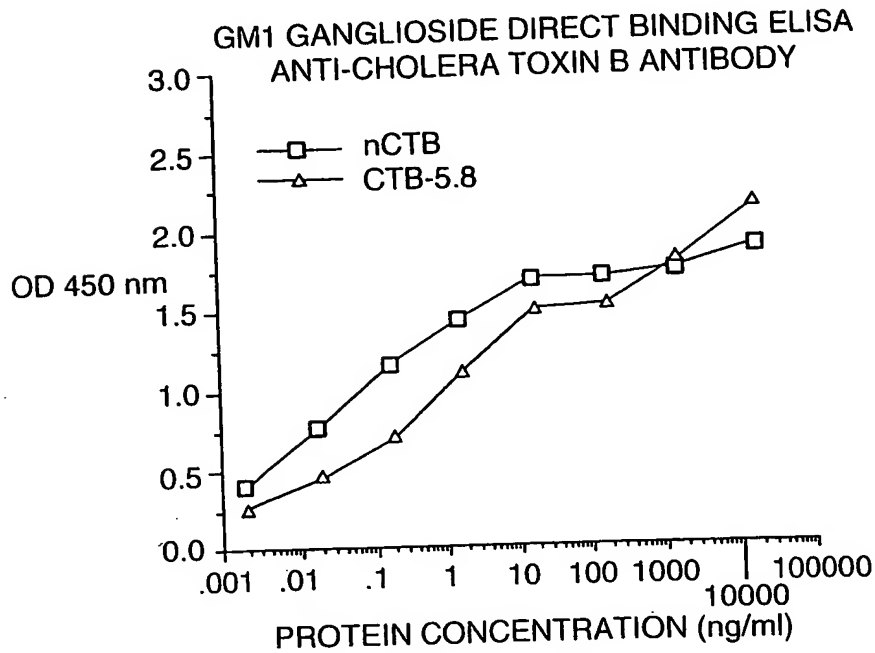


FIG. 14A

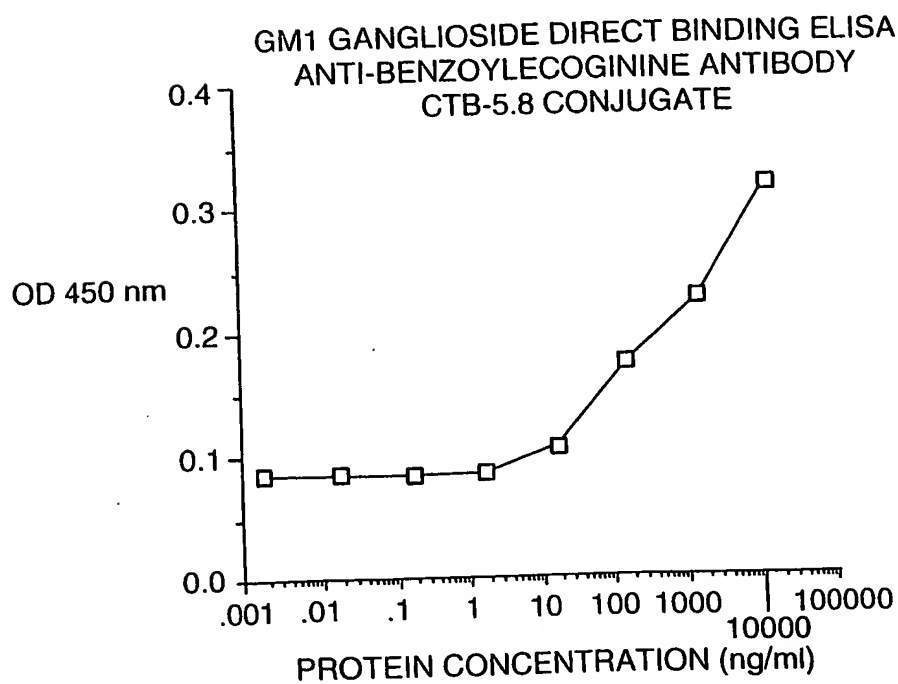


FIG. 14B

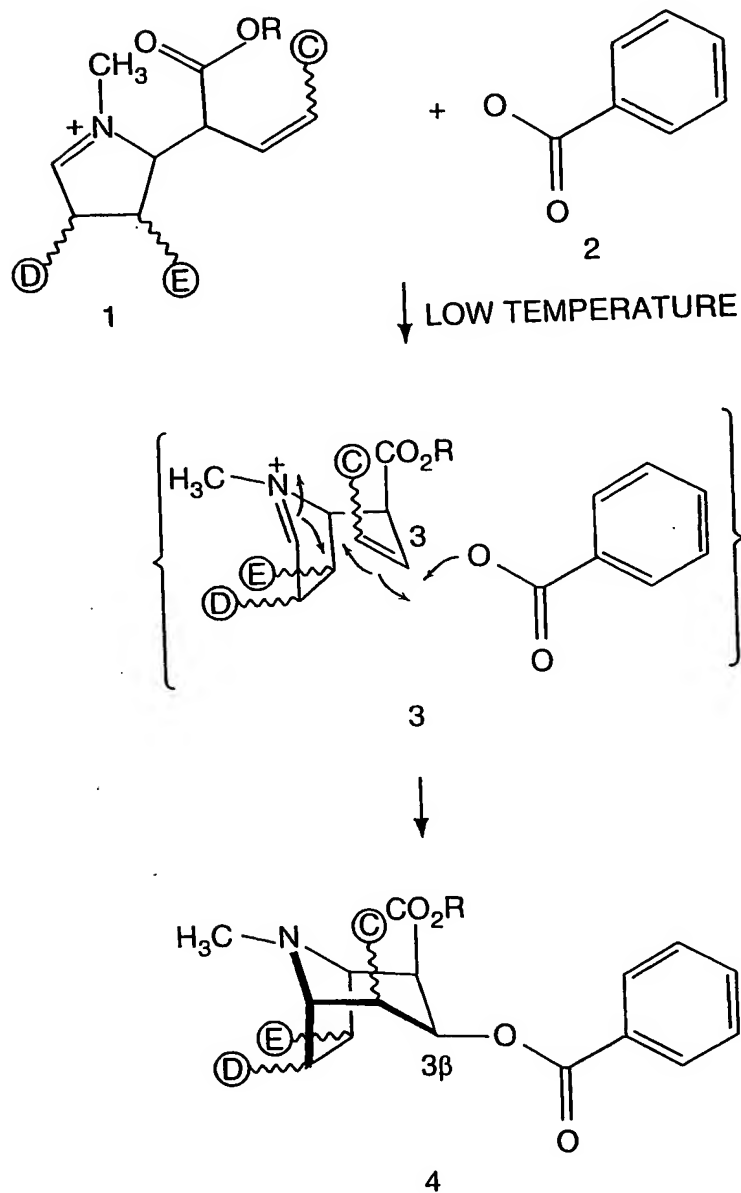


FIG. 15

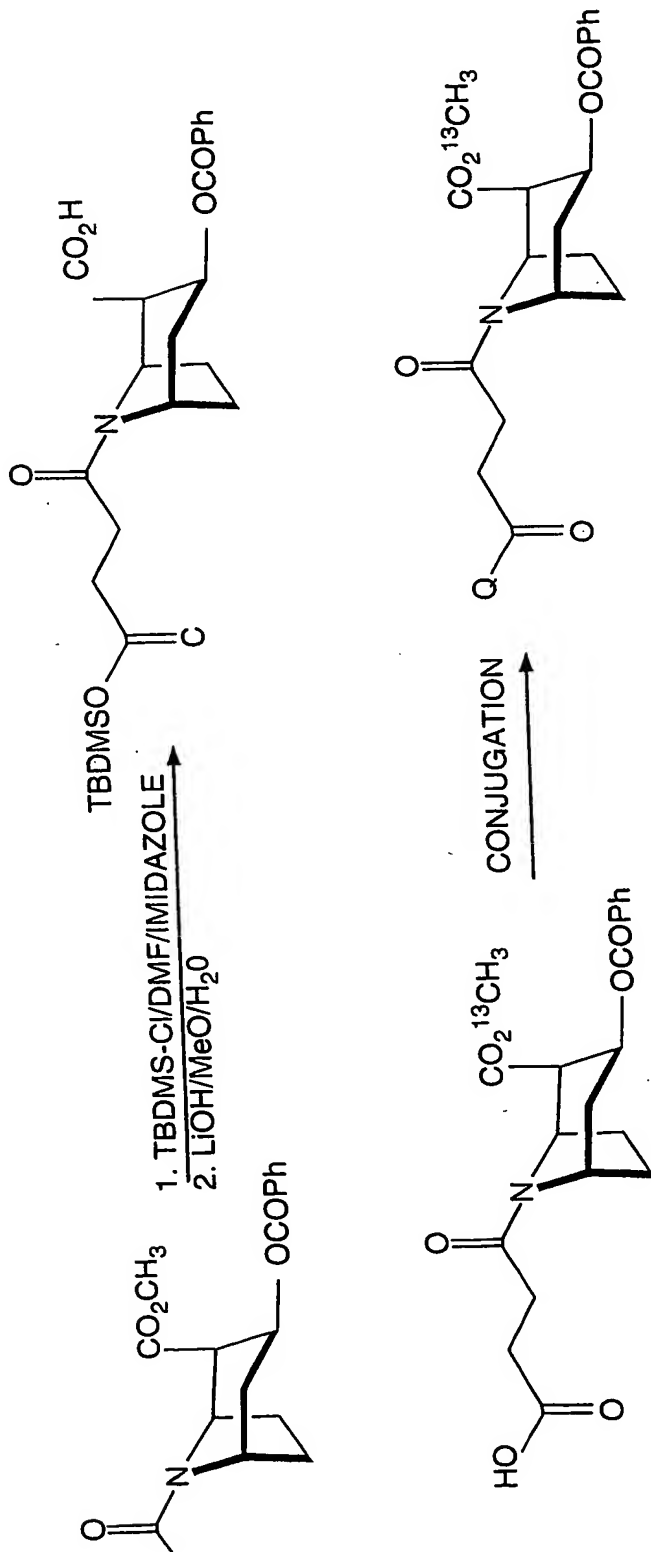


FIG. 16

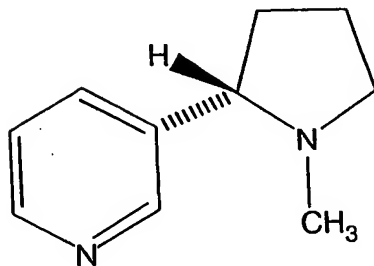


FIG. 17A

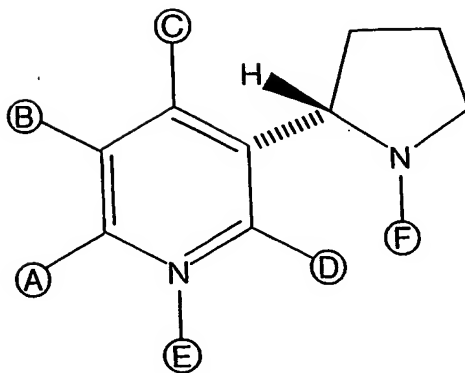


FIG. 17B

	A	B	C	D	E	F
PS-51	CJ1 where Q=COOH or where Q=CJ1.2, wherein Q=T-cell epitope containing carrier.	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	---	CJ0 where Q=CH <sub>3</sub>
PS-52	CJ0 where Q=H	CJ1 where Q=COOH or where Q=CJ1.2, wherein Q=T-cell epitope containing carrier.	CJ0 where Q=H	CJ0 where Q=H	---	CJ0 where Q=CH <sub>3</sub>
PS-53	CJ0 where Q=H	CJ0 where Q=H	CJ1 where Q=COOH or where Q=CJ1.2, wherein Q=T-cell epitope containing carrier.	CJ0 where Q=H	---	CJ0 where Q=CH <sub>3</sub>
PS-54	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	---	CJ3 where Q=OH or T-cell epitope containing carrier, n=2
PS-55	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ1 where Q=H or a T-cell epitope containing carrier n=3	CJ0 where Q=CH <sub>3</sub>
PS-56	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ1 where Q=H or a T-cell epitope containing carrier n=4	CJ0 where Q=CH <sub>3</sub>
PS-57	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ1 where Q=H or a T-cell epitope containing carrier n=5	CJ0 where Q=CH <sub>3</sub>

FIG. 18A

	A	B	C	D	E	F
PS-58	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	CJ1 where Q=H or a T-cell epitope containing carrier n=7	CJ0 where Q=CH <sub>3</sub>
PS-59	CJ11 where Y=NH Q=OH or T-cell epitope containing carrier	CJ0 where Q=H	CJ0 where Q=H	CJ0 where Q=H	---	CJ0 where Q=CH <sub>3</sub>
PS-40	CJ0 where Q=H	CJ11 where Y=NH Q=OH or T-cell epitope containing carrier	CJ0 where Q=H	CJ0 where Q=H	---	CJ0 where Q=CH <sub>3</sub>

FIG. 18B

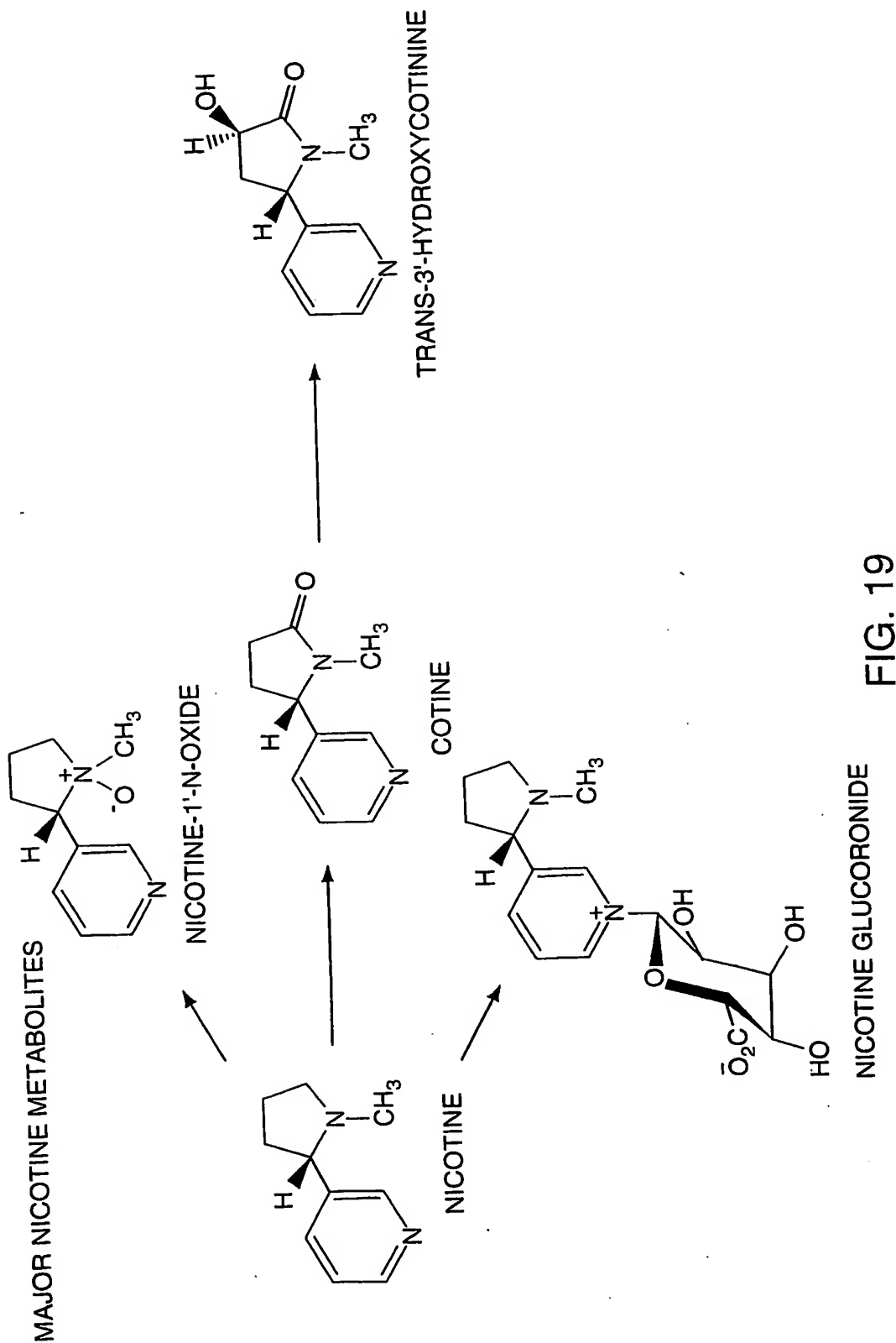


FIG. 19

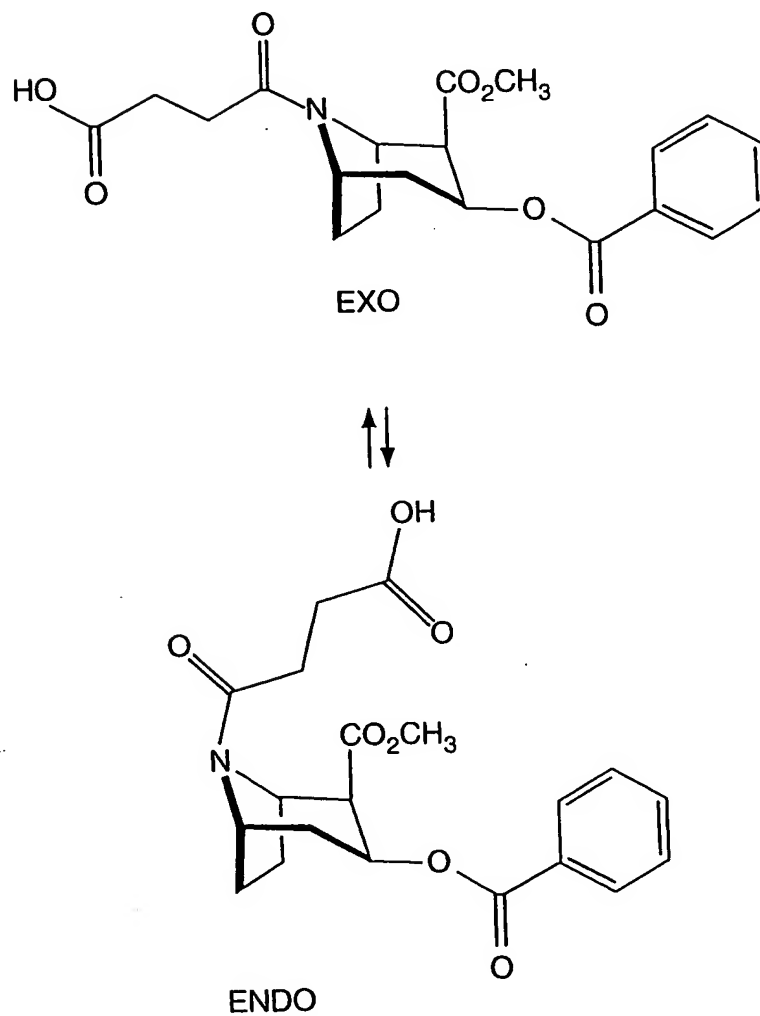


FIG. 20

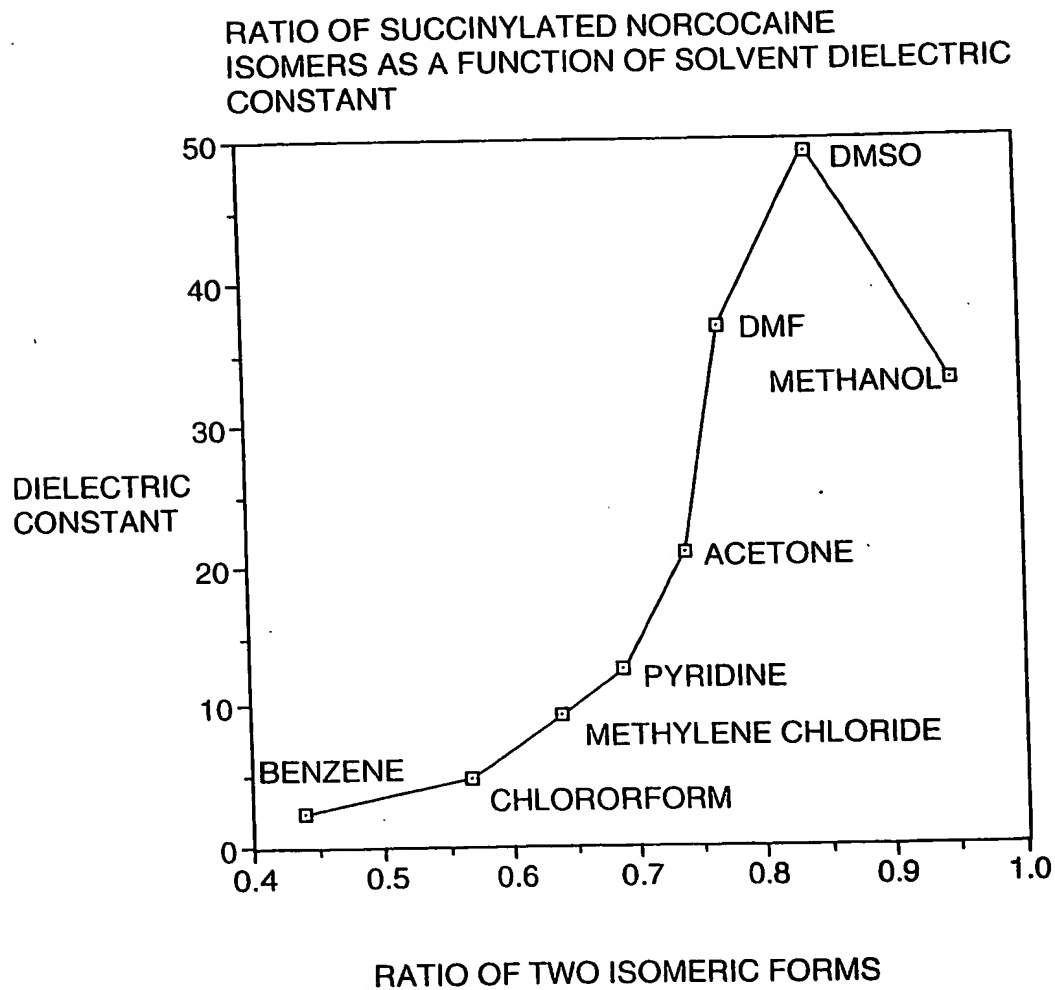
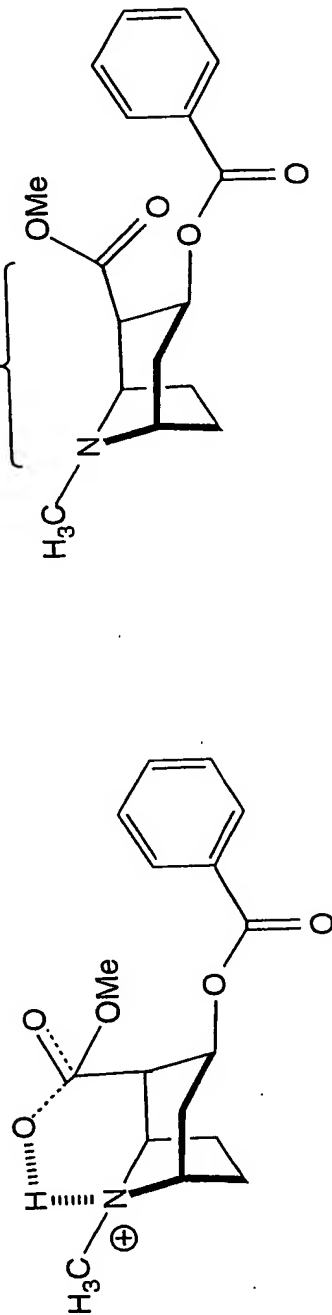


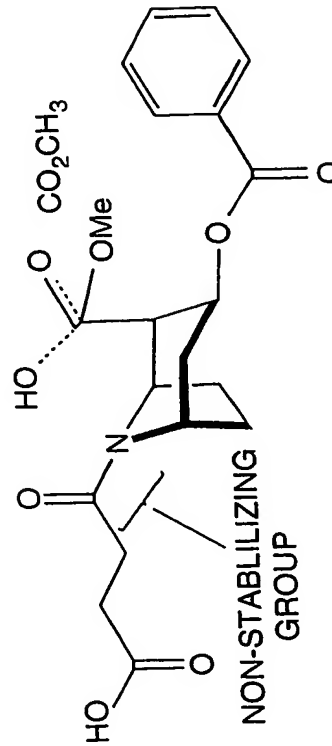
FIG. 21

DISTANCE TOO FAR BETWEEN ESTER AND NITROGEN FOR  
 ENHANCED STABILITY OF INTERMEDIATE



PSEUDOCOCAINE

INTERMEDIATE OF COCAINE HYDROLYSIS



HYDROLYZED SUCCINYLATED NORCOCAINE INTERMEDIATE

FIG. 22

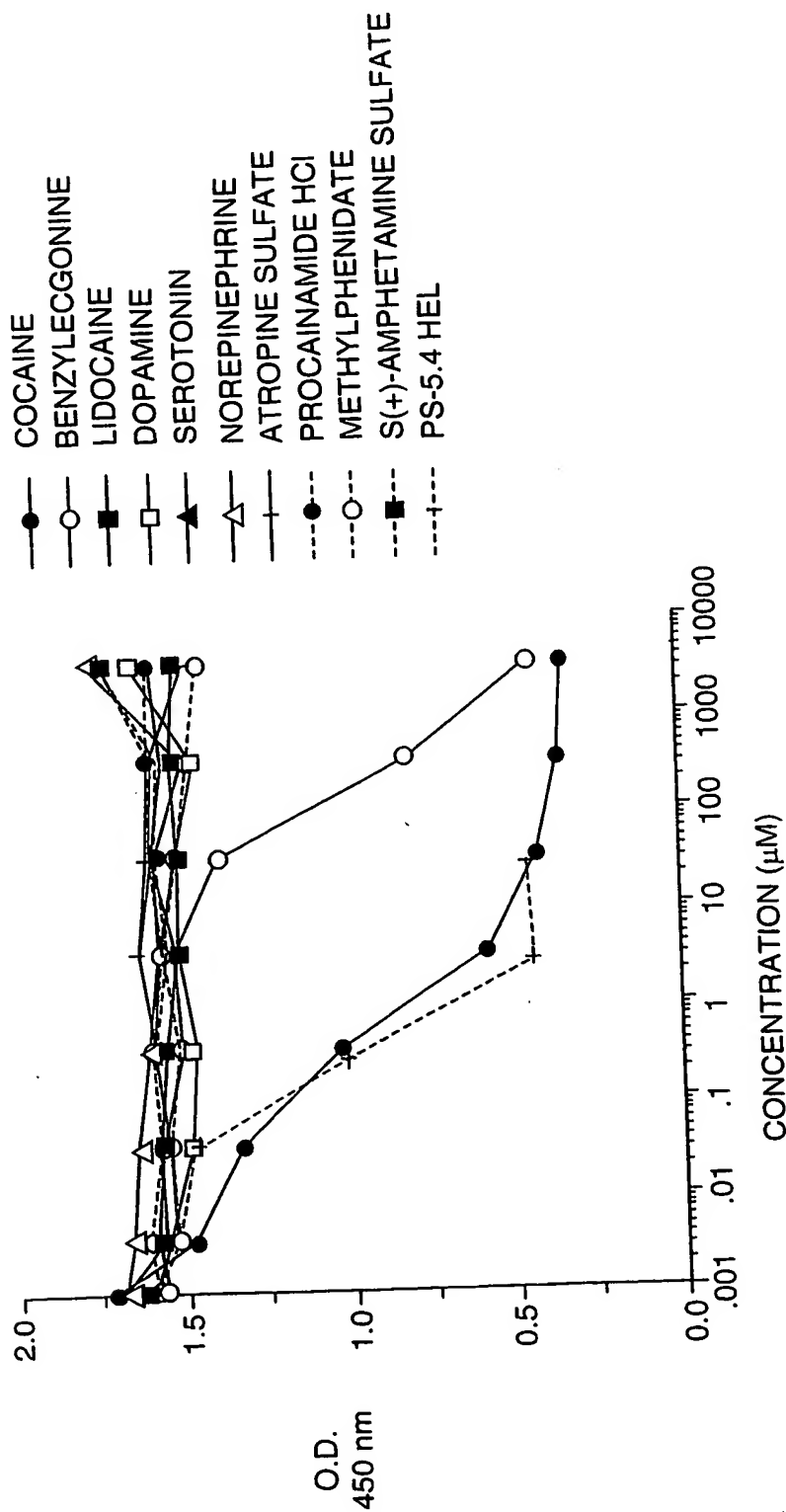


FIG. 23

STRONG ANTIBODY RESPONSES INDUCE  
BY NICOTINE-BSA CONJUGATE

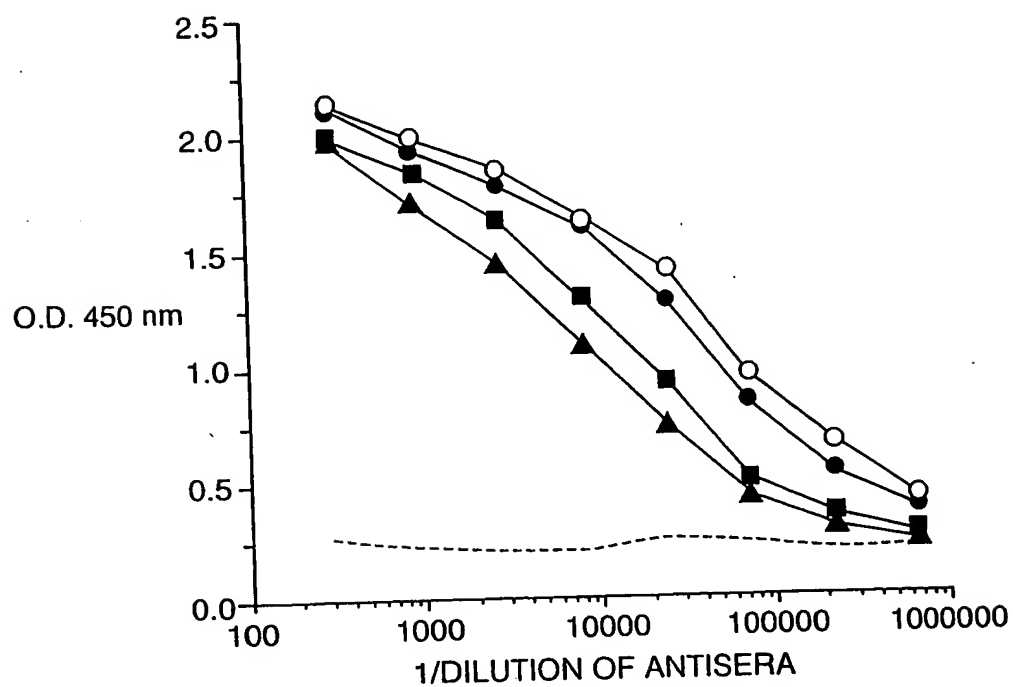
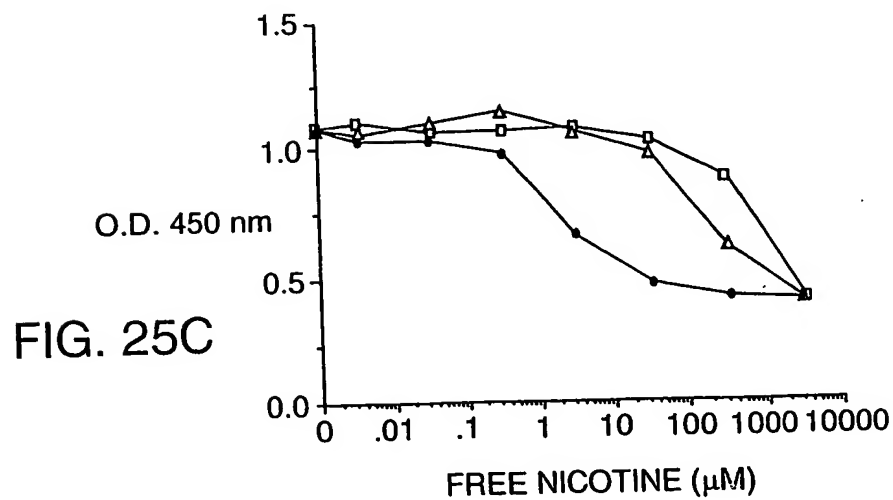
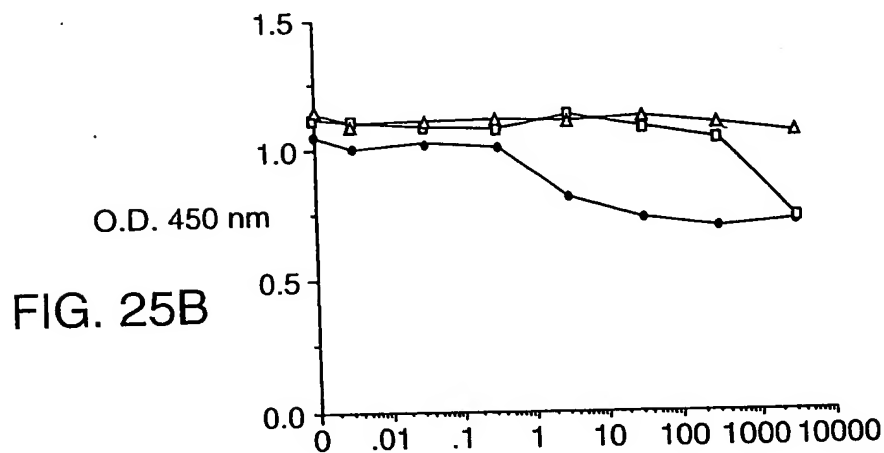
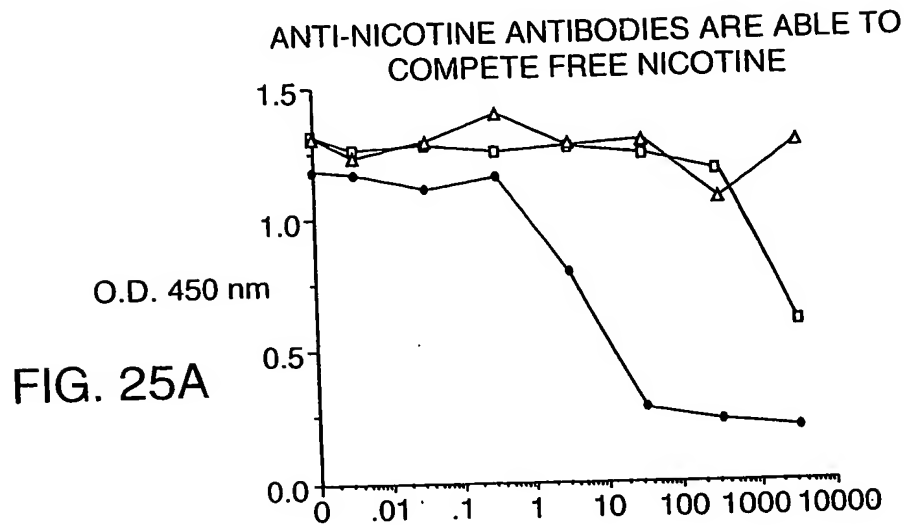
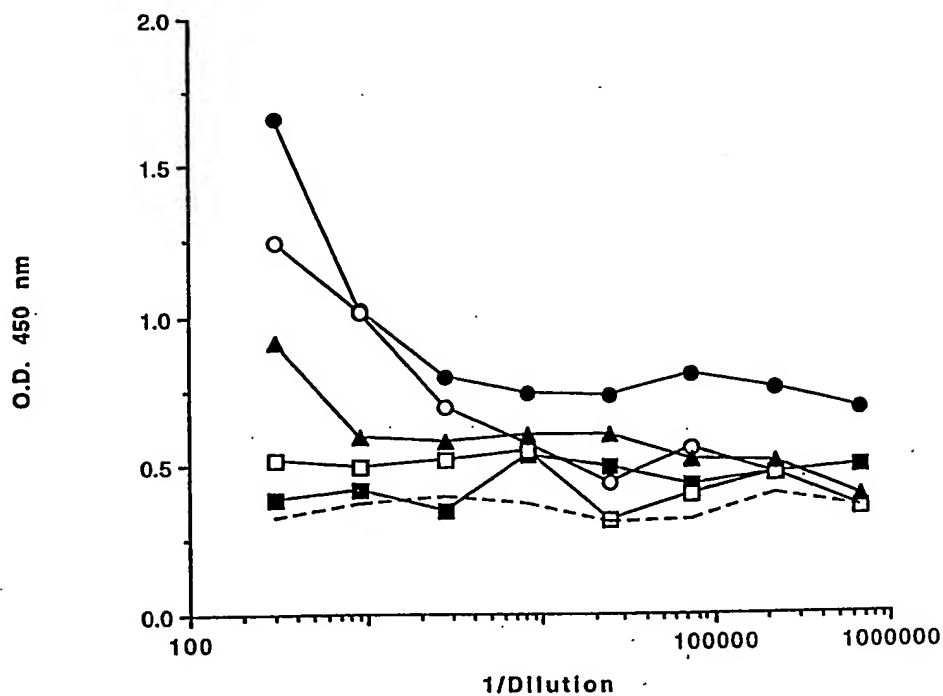


FIG. 24



**Production of anti-cocaine antibodies in Wistar rats****FIG.26**

ANTI-COCAINE ANTIBODIES GENERATED IN WISTAR RATS  
ARE ABLE TO BIND FREE COCAINE

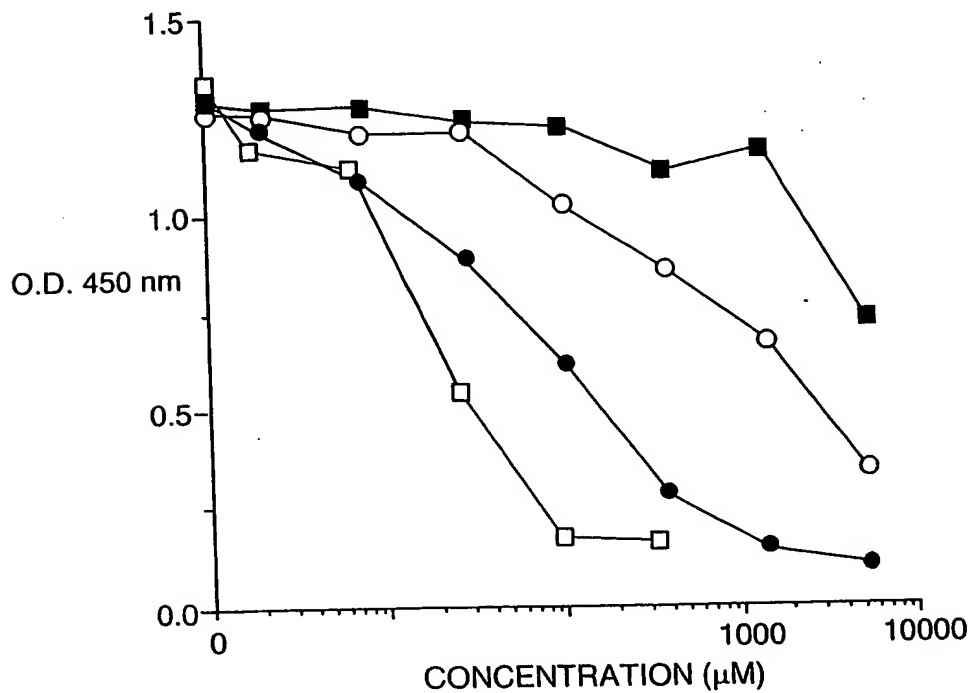


FIG. 27